Effect of the stroke team on the success of intravenous thrombolytic therapy in emergency department

Stroke team in intravenous thrombolytic therapy

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Abstract

Aim: Timely initiation of intravenous thrombolytic therapy (ITT) in ischemic stroke patients reduces long-term neurological impairment and increases the success rate of the treatment. Implementing systems where clinicians establish guideline-based multidisciplinary cooperation is also essential. This study aimed to investigate the effect of door-to-needle time (DTN) in the emergency department (ED) on the early and late clinical courses of patients in cooperation with the neurology clinic.

Material and Methods: The data of the acute ischemic stroke patients who underwent ITT between April 2018 and March 2022 in the ED with inter-clinical coordination were evaluated retrospectively. DTN time, National Health Institute Stroke Scale (NIHSS) scores at admission, 24th hour, pre-treatment, discharge, and 3rd month modified Rankin Scale scores (mRS) of the patients were recorded by the ED physician and neurologist and evaluated statistically.

Results: Of the 102 patients included in the study, 51 were male, and 51 were female. The median age was 75. Of the patients, 45.1% underwent mechanical thrombectomy. The median admission and 24-hour NIHSS scores were 11 and 8, respectively. The median door-to-CT and DTN times were 18.5 minutes and 85.5 minutes, respectively. Patients with DTN times > 60 minutes had higher admission systolic and diastolic blood pressure levels than patients with DTN times < 60 minutes ($p < 0.01$ and $p = 0.015$, respectively). Good functional outcome rates (mRS score 0-2) at discharge and at 3 months were 39.2% and 49.0%, respectively.

Discussion: This study showed that applying ITT with inter-clinical coordination to stroke patients in the ED is associated with a good early clinical outcome.

Keywords

Emergency Department, Neurology, Stroke, Teamwork, Thrombolytic Therapy

Introduction

Early intravenous recombinant tissue plasminogen activator (IV r-tPA) treatment in ischemic stroke patients significantly reduces mortality and long-term neurological disability [1]. Success in intravenous thrombolytic therapy (ITT) depends on how early the treatment is administered.

To determine the need for rapid evaluation and treatment of acute ischemic stroke in hospitals, systems based on guidelines that establish a multidisciplinary collaboration of clinicians have begun to be implemented. However, published studies have shown that despite these systems, differences and inconsistencies exist, and many hospitals lack organizations and teams to effectively diagnose, manage, and treat stroke patients [2].

According to some studies, the time to treatment had a prognostic effect on stroke patients who received ITT at the time [3]. Previous studies have evaluated the treatments used in hospitalized patients with ischemic stroke and their discharge from the hospital. On the other hand, early and late clinical outcomes of ischemic stroke patients in the emergency department (ED) with the cooperation of a neurologist and an emergency medicine physician have not been studied. Therefore, this study aims to evaluate the effect of door-to-needle time (DTN) on the patients' third-month clinical status and mortality, to whom ITT was applied in cooperation with a neurologist in the ED.

Material and Methods

In this study, patients diagnosed with acute ischemic stroke who were treated with ITT in collaboration with an emergency medicine physician and a neurologist in the Department of Emergency Medicine of Sultan 2 Abdulhamid Khan Training and Research Hospital between April 2018 and March 2022, were evaluated retrospectively. To access the data, the protocol numbers of the patients who received the ischemic stroke code according to the ICD-10 diagnostic coding system were obtained from the hospital automation system, and the files were retrieved from the hospital archive.

In our hospital, the treatment process for stroke patients is carried out in the ED and neurology clinic with 24-hour telecommunication between physicians on duty. Patients who presented to the ED within 4.5 hours of the onset of stroke symptoms, had a measurable neurological deficit in physical examination and history, and had an excluded hemorrhage on cranial computed tomography (CT) were evaluated for ITT. Simultaneously with the patients' referral to cranial imaging, a telemedicine consultation process was initiated with the on-duty neurology team, and the suitability and contraindications of all patients in terms of ITT application in the ED were questioned in cooperation with neurologists and emergency medicine physicians.

A common standard data collection form was created, and the patients who were admitted to the neurology clinic after ITT in the ED and whose functional outcomes could be reached at 24 hours, discharge, and three months were included in this study. Patients whose three-month functional outcome could not be reached and who had hemorrhagic transformation (HT) on computerized brain tomography (CBT) were excluded from the study [4].

Stroke severity was measured in all patients according to the National Health Institute Stroke Scale (NIHSS) at admission and 24 hours after treatment. An increase in the NIHSS score of four or more after ITT and bleeding on CBT was considered symptomatic intracerebral hemorrhage (sICH) [5].

Patients diagnosed with ischemic stroke in the ED were divided into two groups based on ITT onset time: 60 minutes and more than 60 minutes. The patients' mRS score, and NIHSS score at admission, imaging time, and DTN were recorded by the ED physician. The neurologist recorded the patients' 24-hour NIHSS scores, discharge, and third-month mRS scores. In the statistical evaluation, the differences in admission, discharge, and the third month were taken into account.

Statistical Analysis

All statistical analyses were conducted using IBM SPSS Statistics 26.0 (IBM Corp, Armonk, NY). All continuous data in this study were expressed as a median, interquartile range (IQR), and range for each value (normality was assessed using the Kolmogorov–Smirnov test). The chi-square test was used to compare categorical variables between two groups, whereas the Mann-Whitney U test was used to compare continuous variables between two groups. Logistic regression analysis was performed to determine the independent predictors. The Hosmer-Lemeshow goodness of fit statistics was used to assess model fit. The 95 percent confidence interval was used to evaluate all analyses, and significance was determined at the $p < 0.05$ level.

Ethical Approval

Approval was obtained from the ethics committee of the University of Health Sciences Haydarpasa Numune Training and Research Hospital (HNEAH-KAEK 2021/KK/222). The results of this study are reported according to the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) recommendations [6].

Results

The study included 102 patients, of whom 51 (50%) were male and 51 (50%) were female. The median age of the patients was 75 years (IQR 19 years, range 40 to 94 years). Seventeen patients (16.7%) died in 30 days in the study population. There was at least one coexisting disease in 87 (85.3%) of the patients, but there was no statistically significant difference between survivors and non-survivors (p = 0.712).

Systolic blood pressure (SBP) and diastolic blood pressure (DBP) at admission in the study population were 154 mmHg (IQR 30, range 111 to 225) and 90 mmHg (IQR 22, range 40 to 139), respectively. SBP and DBP were statistically different between patients with DTN times of ≤ 60 minutes and > 60 minutes (p < 0.01 and p = 0.015, respectively). There were no other statistical differences between admission vital parameters. The median admission and 24th-hour NIHSS scores were 11 (IQR 11, range 2 to 27) and 8 (IQR 13, range 0 to 30). The median door-to-scanner (DTS) and DTN times were 18.5 minutes (IQR 18, range 2 to 95) and 85.5 minutes (IQR 66, range 17 to 205). Admission parameters and clinical characteristics of the patients and DTN groups are shown in Table 1.

Symptomatic intracerebral hemorrhage was observed in 17

Table 1. Admission parameters and clinical characteristics of the patients according to DTN groups.

	Total population, N:102	DTN time ≤ 60 minutes, N:36	DTN time > 60 minutes, N:66	p-value
Age, Median (IQR) [min-max], years	75.0 (19) [40-94]	74.5 (17) [40-94]	75.5 (22) [40-94]	0.273*
Admission SBP, mmHg, Median (IQR)	154 (30) [111-225]	149 (25) [113-200]	156 (42) [111-225]	<0.01*
Admission DBP, mmHg, Median (IQR)	90 (22) [40-139]	83 (16) [40-132]	93 (26) [54-139]	0.015*
Admission NIHSS, (N), (%)				
<5	17 (16.7%)	6 (16.7%)	11 (16.7%)	-
5.15	57 (55.9%)	18 (50.0%)	39 (59.1%)	0.377 †
16-20	18 (17.6%)	11 (30.6%)	7 (10.6%)	0.012 †
21-42	10 (9.8%)	1 (2.8%)	9 (13.6%)	0.094 †
24-Hour NIHSS, (N), (%)				
<5	35 (34.3%)	15 (41.7%)	20 (30.3%)	0.248 †
5.15	39 (38.2%)	15 (41.7%)	24 (36.4%)	0.598 †
16-20	15 (14.7%)	1 (2.8%)	14 (21.2%)	0.012 †
21-42	13 (12.7%)	5 (13.9%)	8 (12.1%)	0.767 †
Admission mRS Score, (N), (%)				
0-2	98 (96.1%)	34 (94.4%)	64 (97.0%)	0.612 †
3.5	4 (3.9%)	2 (5.6%)	2 (3.0%)	0.612 †
Discharge mRS Score, (N), (%)				
0-2	40 (39.2%)	19 (52.8%)	21 (31.8%)	0.038 †
3.5	39 (38.2%)	11 (30.6%)	28 (42.4%)	0.238 †
6	23 (22.5%)	6 (16.7%)	17 (25.8%)	0.294 †
3-Month mRS Score, (N), (%)				
0-2	50 (49.0%)	22 (61.1%)	28 (42.4%)	0.071 †
3.5	21 (20.6%)	7 (19.4%)	14 (21.2%)	0.833 †
6	31 (30.4%)	7 (19.4%)	24 (36.4%)	0.076 †
Time Goals, Median (IQR), minutes				
Symptom-to-door	58.5 (58) [4-230]	47.5 (35) [11-180]	60 (51) [4-230]	0.103*
Door-to-scanner	18.5 (18) [2-95]	15 (11) [5-50]	23 (21) [2-95]	<0.01*
Door-to-needle	85.5 (66) [17-205]	42.5 (19) [17-60]	109 (41) [61-205]	-
Symptom-to-needle	150 (96) [50-320]	90 (52) [50-225]	180 (60) [67-320]	<0.001*
Thrombectomy, (N), (%)	46 (45.1 %)	23 (63.9%)	23 (34.5%)	<0.01 †
Hospitalization, (N), (%)	9 (8.8%)	5 (13.9%)	4 (6.1%)	0.273 †
ICU, (N), (%)	93 (91.2%)	31 (86.1%)	62 (93.9%)	0.273 †
Exitus (30-days), (N), (%)	17 (16.7%)	4 (11.1%)	13 (19.7%)	0.266 †

* Mann-Whitney U test was used to compare differences; †Chi-square test was used for analysis; DBP, diastolic blood pressure; DTN, door-to-needle; ED, emergency department; ICU, intensive care unit; IQR, interquartile range; mRS, modified Rankin Scale; NIHSS, National Health Institute Stroke Scale; SBP, systolic blood pressure.

(16.7%) patients, and comparison of the patients by their sICH is shown in Table 2.

To evaluate factors affecting the good functional outcome (mRS 0-2), a multivariable logistic regression analysis was performed to adjust for baseline clinical characteristics (Table 3).

Discussion

This study was conducted to evaluate the relationship between DTN time and treatment outcomes in patients with acute ischemic stroke who underwent ITT. Within the framework of these studies, it is important to recognize stroke patients in ED and to avoid delays in DTN time. Unlike other studies, our aim in this study was to investigate the relationship between discharge, clinical course, and mortality in patients with DTN times less than or equal to 60 minutes in ITT administration in the ED.

In our study, there was no correlation between demographic characteristics of the patients and risk factors such as

hypertension, DM, hyperlipidemia, CAD history, and DTN time. Therefore, none of the patients' underlying factors could determine DTN time or prognosis. In the study by Navalkele et al. [7] on DTN time in two patient groups with prehospital BP greater than or equal to 185/110 and less than 185/110 in acute ischemic stroke patients, it was shown that high prehospital BP prolongs DTN time. According to the AHA/ASA guidelines, it is recommended to reduce BP below 185/110 mmHg before the intervention, which has been shown to be another common cause of delay in the DTN time [4]. In our study, the mean systolic and diastolic blood pressures at admission were found to be significantly higher in patients with a DTN time >60 minutes, similar to other studies.

Time measurements are important in the interpretation of imaging in ischemic stroke. Current guidelines recommend taking parenchymal imaging within 25 minutes of admission to the ED and interpreting these scans within 20 minutes of taking them [4]. When we evaluated the patients who underwent ITT

Table 2. Clinical characteristics and time goals of patients according to symptomatic intracerebral hemorrhage status.

	Non-sICH Group N:85	sICH Group N:17	p-value
Admission NIHSS, Median (IQR) [min-max]	10 (10) [2-27]	17 (7) [6-23]	<0.01*
24-Hour NIHSS, Median (IQR) [min-max]	6 (10) [0-30]	19 (9) [5-25]	<0.001*
Admission mRS Score, (N), (%)			
0-2	82 (96.5%)	16 (94.1%)	0.524 ₸
3.5	3 (3.5%)	1 (5.9%)	0.524 ₸
Discharge mRS Score, (N), (%)			
0-2	40 (47.1%)	-	<0.001
3.5	33 (38.8%)	6 (35.3%)	0.785 ₸
6	12 (14.1%)	11 (64.7%)	<0.001 ₸
3-Month mRS Score, (N), (%)			
0-2	50 (58.8%)	-	<0.001
3.5	16 (18.8%)	5 (29.4%)	0.335 ₸
6	19 (22.4%)	12 (70.6%)	<0.001 ₸
Time Goals, Median (IQR), minutes			
Symptom-to-door	60 (53) [4-230]	35 (35) [11-120]	0.024*
Door-to-scanner	18 (16) [2-95]	25 (25) [5-60]	0.299*
Door-to-needle	87 (68) [17-205]	83 (66) [35-130]	0.798*
Symptom-to-needle	155 (95) [50-320]	120 (93) [60-220]	0.064*
Exitus (30-days)	10 (11.8%)	7 (41.2%)	0.008*

* Mann-Whitney U test was used to compare differences; ₸ Chi-square test was used for analysis; IQR, interquartile range; mRS, modified Rankin Scale; NIHSS, National Health Institute Stroke Scale; sICH, symptomatic intracerebral hemorrhage.

Table 3. Unadjusted and adjusted logistic regression modeling for odds of achieving good functional outcome (mRS 0–2 at 90 days).

Variables	Unadjusted		Adjusted	
	Odds ratio (95% CI)	p-Value	Odds ratio (95% CI)	p-Value
Age	0.958 (0.93-0.99)	0.006	0.969 (0.93-1.01)	0.111
Oxygen saturation	1.225 (1.05-1.43)	0.01	1.280 (1.04-1.58)	0.019
Admission NIHSS	0.807 (0.74-0.88)	<0.0001	0.807 (0.73-0.89)	<0.001
Door-to-needle time	0.995 (0.99-1.01)	0.303	0.993 (0.98-1.01)	0.262

CI, confidence interval; mRS, modified Rankin Scale; NIHSS, National Health Institute Stroke Scale.

according to the duration of DTS, the median DTS time was 18.5 minutes after pre-evaluation by the emergency medicine physician after admission to the ED, reaching the ideal DTS of 20 minutes.

In the study by Sari Aslani et al. [8], in which they evaluated mortality in patients with acute ischemic stroke who underwent ITT, the mean NIHSS scores before ITT were 11 at admission and 6.3 at discharge. Also, the study by Dong et al. [9] stated that the use of ITT was effective in reducing the NIHSS score (admission score 10.5 and discharge score 5.1). Similar to other studies, in our study, the admission NIHSS scores range was 2–27 points, the median was 11 points, and the median 24th-hour NIHSS score decreased to 8 points (range 0–30), and these findings were consistent with the literature. When we evaluated the admission NIHSS score according to their correlation with DTN time, the proportion of patients with moderate stroke who had an admission NIHSS score of 16–20 was higher (30.6%

vs. 10.6%) in the patients with a DTN time of <60 minutes compared to ones with a DTN time of > 60 minutes (p = 0.012). Moreover, among patients with a 24th-hour NIHSS score of 16–20 there was a higher proportion of patients with a DTN time of > 60 minutes than those with a DTN time of < 60 minutes (21.2% vs. 2.8%, p = 0.012). These findings show that patients with a high NIHSS score at admission received ITT faster, and patients with a high NIHSS score at 24 hours initially received ITT later.

In our study, we also evaluated the effectiveness of the NIHSS score in predicting sICH. Studies have shown that among acute ischemic stroke cases, there is a statistically significant relationship between the development of hemorrhagic transformation and the NIHSS score. The NIHSS score was found to be correlated with cerebral infarct volume [10]. Mahdy et al. [11] found a significant positive correlation between sICH volume and NIHSS scores in 120 cases with sICH (p<0.001). Similarly, when Liu et al. [12] prospectively evaluated 1207 patients with acute ischemic stroke, they reported that patients who developed HT had significantly higher NIHSS scores. In our study, the median NIHSS scores before treatment were 17 in the group with sICH and 10 in the group without bleeding, and the difference was significant (p < 0.01). The median post-treatment NIHSS scores were 19 in the sICH group and 6 in the non-sICH group, and the difference was also significant (p < 0.001).

In the prospective, multicenter Standard Treatment with Alteplase to Reverse Stroke (STARS) study by Albers et al. [13] in 57 medical centers in the United States, the 30-day mortality rate was 13%. In the National Institute of Neurological Disorders and Stroke (NINDS) study on the effectiveness of ITT in acute ischemic stroke, short-term mortality was 17% in patients who underwent ITT [14]. In our study, the 30-day mortality rate was 16.7% (N: 17), similar to the previous studies. When we also looked at the relationship between mortality rate and DTN time in our study, the 30-day mortality rate was higher in patients with a DTN time longer than 60 minutes compared to the group with a DTN time of less than 60 minutes (19.7% vs. 11.1%).

In a meta-analysis of 13 studies examining good functional outcomes in patients undergoing ITT and endovascular recanalization therapy, Mistry et al. [15] defined a good functional outcome as an mRS of 0–2 at the third month and found an mRS at the third month to be between 39% and 51%. In our study, the rates of good functional outcome at discharge and the third month (mRS 0-2) were 39.2% and 49.0%, respectively, similar to previous studies. When we evaluated the relationship between good functional outcome rate and DTN time, we found that the DTN time of the group with mRS 0-2 at discharge was significantly shorter, and the shortening in DTN time was associated with good clinical outcomes (p = 0.038).

In our study, we also found that the NIHSS score at admission was effective in predicting a good outcome, but the change in DTN time was not significant in the third-month clinical status in the multivariate logistic regression analysis we performed to understand the effect of the change in DTN time and the basic clinical features on the third-month outcome better (p = 0.262). These findings supported the result that shortening the DTN time was effective for early-stage good clinical outcomes,

was not significantly associated with late-stage good clinical outcomes, and that the admission NIHSS score could be attributed to a good outcome in treatment.

The median value of DTN time in our study was 85.5 minutes, which was longer than the results obtained in Askari-Majdabadi et al.'s acute ischemic stroke management study in Iran (70 minutes) [16]. It can be thought that the long duration of DTN in our study may be due to hesitations arising from complications that may develop and the application of stroke protocols.

Limitations

This study has several limitations. First of all, it is an important limitation that the study was single-centered and retrospective. However, in an ED with high numbers of ischemic stroke patients, all consecutive patients meeting the criteria for ITT were included in the study, thus limiting patient selection bias.

Conclusion

This study showed that DTN time is associated with a good early clinical outcome in ischemic stroke patients undergoing ITT. Therefore, patients with ischemic stroke symptoms should be recognized early, and all attempts should be made to reduce the time of DTN through experience. In addition, high late mortality rates may be related to stroke protocols applied during the elapsed time of DTN and hesitations due to the development of sICH. As a result, we believe that increasing experience in the early administration of ITT in the ED through inter-clinical communication and possibly monthly case-evaluation meetings will have a significant impact on good clinical outcomes in stroke patients.

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